Fibromyalgia: clinical and occupational aspects

Milton Helfenstein Junior[1], Marco Aurélio Goldenfum[2], César Augusto Fávaro Siena[3]

[1] PhD in Rheumatology; Assistant Doctor, Universidade Federal de São Paulo (Unifesp), São Paulo, SP, Brazil
[2] MSc Student in University Teaching, National Technological University of Buenos Aires, Argentina; Coordinator, Postgraduate Program in Occupational Medicine and Medical Inspections, Escola Superior de Gestão e Ciências da Saúde de Porto Alegre, Porto Alegre, RS, Brazil
[3] Federal Court Medical Expert of Ribeirão Preto, Ribeirão Preto, SP, Brazil

Summary

Fibromyalgia (FM) is a clinical syndrome commonly observed in daily medical practice and its etiopathogenesis is still unclear. As it is characterized by chronic musculoskeletal pain associated with several symptoms, FM may be confused with several other rheumatic and nonrheumatic diseases when they course with pictures of diffuse pain and chronic fatigue. FM treatment should be multidisciplinary, individualized, count on active participation of the patient, and based on combined pharmacological and non-pharmacological modalities. It is found both in work and non-work settings, and there is no scientific evidence in the literature showing that FM might be caused by occupation. FM seldom leads to incapacity to work. In cases where pain or fatigue do not respond to appropriate treatment, reaching significant levels, a short period away from work can be considered. As FM is a relevant subject, this review article was based on exploratory, qualitative and bibliographic investigation, aiming to study the main clinical and occupational aspects of FM, emphasizing the theoretical-conceptual background and the experience of specialists.

Keywords: Fibromyalgia; review; rheumatology; occupational medicine; referred pain.

Study conducted at the Discipline of Rheumatology, Escola Paulista de Medicina, Universidade Federal de São Paulo
São Paulo, SP, Brazil

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Correspondence to:
Milton Helfenstein Junior
Rua João de Lacerda Soares, 90
Brooklin
São Paulo – SP, Brazil
CEP: 04707-010
m.helfen@terra.com.br

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Introduction

Fibromyalgia (FM) can be described as a painful clinical syndrome associated with other symptoms, and it is also termed fibromyalgia syndrome. In this review, the term fibromyalgia, used in the International Classification of Diseases (ICD), has been adopted.

Although it has been recognized for a long time, FM has been seriously studied for the last four decades. FM was not considered a well-defined clinical entity until the 1970's, when the first reports on sleep disturbances were published. The concept of FM was introduced in 1977, when anatomical sites with excessive pain sensitivity were described; they were termed tender points. Sleep disturbances, including those experimentally induced, were also documented, possibly reproducing pain and muscular sensitivity symptoms seen in this chronic pain syndrome[1].

The term fibromyalgia is derived from the Latin word *fibro* (fibrous tissue, present in ligaments, tendons and fasciae) and from the Greek words *mio* (muscular tissue), *algos* (pain), and *ia* (condition). It was first proposed by Yunun et al. in 1981, aiming to replace the term fibrositis[2], hitherto used to name a particular type of rheumatism characterized by the presence of tender indurated muscular points, which were understood as having no tissue inflammation[3].

In the 1980's, several diagnostic criteria based on systemic disease exclusion, presence of certain symptoms, and tender points on physical examination were suggested.

In 1990, a committee from the American College of Rheumatology (ACR) defined the FM classification criteria as the presence of a clinical history of widespread pain, affecting the axial and peripheral skeleton, above and below the waist, and with a duration > 3 months; physical examination pain elicited by application of a 4 kg/cm^2 force to at least 11 of the following 18 *tender points* (9 pairs): 1) suboccipital muscle insertions; 2) ligaments of intertransverse spaces C5-C7; 3) trapezius upper border; 4) supraspinatus muscle origins; 5) pectoral muscle junction with the second rib costocondral junction; 6) 2 cm distal to the elbow lateral epicondyle; 7) upper outer quadrant of buttocks, below the iliac spine; 8) muscle insertions at the femoral trochanter; 9) fat pad, slightly above the knee midline[4].

The current diagnostic criteria do not include tender points; however, they consider symptoms not related to the locomotor system. In addition to musculoskeletal pain, they assess the syndrome's severity and are useful to establish the diagnosis[5].

Considering the subject's relevance, this review aims to discuss the main clinical and occupational aspects of FM.

Methods

This review article is derived from a qualitative, exploratory and bibliographic investigation performed in the electronic libraries SciELO and PubMed, emphasizing the theoretical-conceptual background and the experience of specialists. The keywords "fibromyalgia", "review", "rheumatology", "occupational medicine", and "referred pain" were searched. Moreover, a manual search of references from selected articles was performed so that papers not mentioned in the databases could be found. The references contributing to meet the search target, i.e., review of the main clinical and occupational aspects of FM, were selected from the material retrieved. The investigation was closed only when signs of search theme theoretical saturation were found.

Epidemiology

FM occurs at any age and is much more often diagnosed in females. A study conducted by the American College of Rheumatology found an FM prevalence of 3.4% for females and 0.5% for males, with an estimated prevalence of 2% for both genders[6].

The first studies dedicated to FM prevalence were reported in the 1980's, but the diagnostic criteria were different, albeit similar to the current criteria. The results ranged from 2.1% in private practices, 5.7% in outpatient facilities, 5% to 8% for inpatients, and as high as 14% to 20% in rheumatology outpatient settings[7].

A Brazilian study determined a prevalence of 2.5% in the population, with the majority of cases identified in females, of whom 40.8% were aged 35 to 44 years[8]. In some European countries, FM rates found in the adult population were as high as 10.5%[9].

FM is a condition commonly seen in daily clinical practice and one of the main causes for medical visits linked to the musculoskeletal system; it is considered the second main rheumatologic disorder, surpassed only by osteoarthritis[10].

Despite the good prognosis for this painful condition, patients with FM consume huge amounts of financial resources in public or private health care both for treatment and diagnostic investigation.

The magnitude of economic and financial impact of FM on society is evidenced in an American study reported in 2007, finding an annual cost of USD 9,573 per patient, and representing an expenditure three to five times higher than that of the general population[11].

Likewise, a survey conducted in the Netherlands identified a mean annual cost of € 7,813 per patient with FM, € 8,553 for chronic low back pain, and € 3,205 for ankylosing spondylitis – the latter amount was calculated before biologics were approved for ankylosing spondylitis treatment[12].

Assuming that FM affects 3% of the population, according to statistical data, and using data from demographical studies, these estimates can be translated into an incremental annual cost of about €12 billion for a population of 80 million, with € 960 million (8%) representing the costs of drug therapy[13].

Etiopathogenesis

FM etiology and pathophysiology are still nuclear. The current hypotheses focus on the central mechanisms of pain modulation and amplification in the genesis of FM. A pathophysiological model integrating many of the ideas found in literature has been accepted; it suggests that the primary disorder in FM would be a change in some central mechanism of pain control, possibly resulting from a neurotransmitter dysfunction. Such neurohormonal dysfunction would include either an inhibitory neurotransmitter deficiency in spinal or supraspinal levels (serotonin, enkephalin, norepinephrine, and others) or an excitatory neurotransmitter hyperactivity (substance P, glutamate, bradykinin, and other peptides). Both conditions might be present. These dysfunctions could be genetically predetermined and triggered by a nonspecific stress, such as a viral infection, psychological stress, or physical trauma[14].

The hypothalamic-pituitary-adrenal axis and the sympathetic nervous system, comprising the main systems of stress response along with their interactions with neurohormonal dysfunctions, are also implicated in the pathophysiology. Susceptibility to FM development seems to be influenced by environmental, hormonal, and genetic factors[15,16], causing changes at the neurohormonal receptors level. An acute stressor could trigger the development of a disordered hypothalamic-pituitary-adrenal axis through unclear mechanisms, possibly involving the sympathetic nervous system and the serotonergic system. Thus, the hypothalamic-pituitary-adrenal axis is believed to play a role in mediating and perpetuating FM symptoms[17].

Diagnosis

FM diagnosis is notably clinical[5]. In addition to diffuse pain in skeletal muscle and the physical examination finding of multiple tender points, most patients with FM also report fatigue, muscle stiffness, pain after exertion, and sleep disturbances. Symptoms of depression, anxiety, memory deficit, inattention, tension headache or migraine, dizziness, vertigo, tingling, symptoms consistent with irritable bowel syndrome or restless feet syndrome, are among several other symptoms not related to the locomotor system[18]. Generalized chronic pain, however, is a cardinal symptom. Myalgia may often show a migratory characteristic responding to biomechanical stress or trauma[19].

Despite having too low diagnostic accuracy to be considered classification criteria, sleep disturbances occur in up to 100% of patients with fibromyalgia and are highly variable. Sleep disturbances are characterized by difficulty in sleep induction, too many awakenings during the night, and a sense that the sleep is not restorative. Sleep disturbances evoke adverse consequences, such as cognitive deficits, morning tiredness, and tendency towards triggering psychiatric disorders[20,21].

The psychological profile of patients with fibromyalgia is associated with perfectionism, severe self-criticism, and obsessive search for details[22]. The high depression prevalence among patients with fibromyalgia is noteworthy[23-25].

Depression characteristics, such as fatigue, guilt feelings, low self-esteem, and victimization lead to a symptom flare and impair the patient's coping strategies toward the disease[26].

So far, there are no specific laboratory tests to confirm the FM diagnosis. The patients have normal inflammatory activity tests and imaging studies[27].

Differential diagnosis

FM may be confused with several other diseases when they course with diffuse pain pictures and chronic fatigue.

The patient with hypothyroidism can have a clinical picture mimicking FM. Thus, as these patients are approached, thyroid function assays are recommended. The literature describes FM clinical picture as an initial manifestation of hypothyroidism[28]. However, there is no evidence that stabilizing thyroid function would dispel the FM picture, and there is no evidence that most patients with FM have a thyroid dysfunction.

Another hormone disorder possibly causing diagnostic confusion with FM is primary hyperparathyroidism. This disorder results from a parathyroid adenoma (monoclonal origin) in 80% to 90% of cases. In nearly all remaining cases, it results from hyperplasia in the four parathyroids (polyclonal origin). In addition to bone (bone pain, pathological fractures, cortical osteopenia, bone cysts, and osteitis fibrosa cystica) and kidney (renal colic, nephrolithiasis, and nephrocalcinosis with kidney failure) manifestations, which are classically part of the disease, unspecific symptoms, such as fatigue, emotional disorder, neuropsychiatric abnormalities and muscular aches may be present, mimicking the clinical picture of FM[29].

Vitamin D deficiency with secondary hyperparathyroidism may cause bone and muscular pain sometimes misinterpreted as FM[30].

In certain settings, osteomalacia can be part of differential diagnosis, as a number of patients have an onset with weakness, muscular pain, and bone tenderness before the radiologic and metabolic manifestations are seen[31]. Polymyalgia rheumatica is another condition that must be remembered in FM differential diagnosis, despite the typical involvement of the pelvic and scapular girdles and the significant elevation of erythrocyte sedimentation rate[32]. The fact that patients with polymyalgia rheumatica have a satisfactory and rapid response to low-dose oral corticosteroids can contribute to diagnostic elucidation. However, muscular ache, the predominant characteristic in this illness, might confuse a less attentive practitioner, particularly when muscular ache is diffuse.

In some cases, polymyositis (as well as other myositis) may be confused with FM. In this disease, it is important to remember that the main complaint is weakness rather than muscular pain. This weakness is characteristically insidious, symmetrical, and progressive, particularly at the scapular and pelvic girdles. It is painful in approximately 15% to 30% of cases. Patients may have arthralgia, similar to FM patients. Other clinical manifestations of muscular inflammatory disease, along with laboratory abnormalities, particularly high muscle enzymes, lead to the correct diagnosis[33].

Some autoimmune collagen diseases, particularly rheumatoid arthritis and systemic lupus erythematosus, may initially manifest as diffuse pain and fatigue, leading to FM misdiagnosis. In other situations, patients with established rheumatoid arthritis or systemic lupus erythematosus, with the various clinical and laboratory manifestations of these illnesses, may simultaneously present with a FM clinical picture. Despite the appropriate therapeutic response of the inflammation, painful complaints may remain. In these cases, synovitis disappears and inflammatory activity tests are normalized, with the concomitant maintenance of a FM clinical picture, coursing independently of the underlying disease. In one study, fibromyalgia coexistence was found in 12% of patients with rheumatoid arthritis[34]. Not infrequently, Sjögren syndrome may have, as an initial manifestation, symptoms of diffuse and unspecific muscle pain accompanied by tiredness, making the diagnosis more difficult until laboratory parameters and other clinical characteristics are established[35].

Certain adverse reactions to drugs may cause diffuse myalgia, thus confusing clinical follow-up. Among these drugs, H2 receptor blocking agents (used in peptic disease), fibrates, and statins (used in the treatment of dyslipidemia)[36] should be mentioned. Illicit drug users may experience similar reactions to a FM clinical picture, particularly patients using cocaine and *Cannabis*. Patients with a history of alcoholism may also have muscle pain during either the alcohol abuse period or the withdrawal period[37].

Certain infections, in particular hepatitis C, human immunodeficiency virus (HIV), and Lyme disease, may cause diffuse muscular pain, making diagnosis more difficult, mainly when fever and other signs are not found[38]. Serum analysis can contribute to elucidate some cases.

Patients who underwent long-term corticosteroid therapy, irrespective of the reason, can experience corticosteroid withdrawal, particularly if the drug cessation has been abrupt or inappropriate. These patients can experience diffuse muscle pain, rapidly responding to corticosteroid reintroduction[39].

Another condition that must be accounted for in FM differential diagnosis is paraneoplastic syndrome. Obviously, there are other signs directing the correct clinical reasoning in this picture. However, in rare situations, a paraneoplasm may manifest with a clinical picture similar to FM and issue an important diagnostic challenge, particularly in the case of bronchogenic carcinoma[40].

Chronic fatigue syndrome should also be included into the differential diagnosis. Low fever or recurring pharyngitis history, in addition to lymphadenopathy, can contribute to clarify the diagnosis. In chronic fatigue syndrome, tiredness predominates, while diffuse pain predominates in fibromyalgia[41].

Possibly the greatest diagnostic challenge is differentiating FM from psychogenic rheumatism. In certain situations, the patient's clinical picture purely expresses a psychiatric disorder, particularly depression. Depression is known to occur more commonly in fibromyalgia than in controls or even in patients with rheumatoid arthritis[42]. About half of patients with FM have had a depression episode at some time in their lives. Many depression symptoms, such as tiredness, energy loss, discouragement, and sleep disturbances, are identical to those in FM. Maybe this is why many authors consider fibromyalgia as a depression manifestation. However, it is important to keep in mind that a large number of patients with fibromyalgia have neither depression nor any other psychiatric disorder component[43].

It is also important to note that sometimes patients with fibromyalgia have been misdiagnosed as having RSI/WRMD (repetition strain injury/work-related musculoskeletal disorders). In an investigation conducted in the Discipline of Rheumatology at Escola Paulista de Medicina, 103 patients with an initial diagnosis of repetition strain injury (RSI) or work-related musculoskeletal disorder (WRMD), all of them involved in a labor dispute, were studied. Among these 103 patients, 73

were found to meet diagnostic criteria for FM and they had no evidence of tissue injury[44].

Finally, RSI and WRMD cannot be widely pointed out as a disease, but they are acronyms embodying a heterogeneous group of musculoskeletal disorders having a work agent as one of the required causes for their appearance. It is important to point out that FM is not a RSI or a WRMD.

Treatment

To this day, the lack of knowledge about FM etiopathogenesis prevents a totally effective treatment.

FM treatment should be multidisciplinary, individualized, count on the patient's active participation, based on combined non-pharmacological and pharmacological therapy and should be designed according to the intensity and characteristics of symptoms. It is important that biopsychosocial issues involved in the context of illness are also considered.

As an initial part of treatment, patients are provided with basic information about FM and treatment options, and are instructed about pain control and self-control programs.

FM drug therapy, in addition to pain control, aims to induce a better quality sleep and treat associated symptoms, such as depression and anxiety.

Nonsteroidal anti-inflammatory drugs (NSAIDs) should not be used as first-line drugs in patients with FM[45]. Although there is no evidence of inflammation, NSAIDs used in treating more prominent painful complaints act satisfactorily on FM-associated symptoms, such as headache and joint pain[46].

Corticosteroids are not a part of the therapeutic resources used in FM[47].

In Brazil, two out of three drugs approved by the Food and Drug Administration (FDA) to treat FM are available: pregabalin and duloxetine. Pregabalin is a calcium channel modulating agent, reducing the release of excitatory pain neurotransmitter release at nervous endings, particularly substance P and glutamate. Studies show significant relief of pain, fatigue, anxiety, and sleep disturbances by using this drug[48]. Duloxetine is a serotonin and noradrenalin reuptake inhibitor that also has shown to be effective in reducing pain and improving functional capacity in FM regardless of the presence of depression[49].

Tricyclic antidepressants, especially amitriptylin and cyclobenzaprine, ingested two to three hours before bedtime, can be effective in decreasing the pain and improving the sleep, as well as enhancing the functional capacity[50,51].

Many other drugs were studied, but the results were usually less satisfactory[52].

Non-pharmacological treatment has a crucial role in managing FM symptoms[53].

FM patients benefit from physical activity. Several reasons justify the encouragement of physical activity in this syndrome: increased levels of serotonin and other inhibitory neurotransmitters; increased GH (growth hormone) production; hypothalamic-pituitary-adrenal axis and autonomous nervous system regulation; increased capillary density; increased myoglobin count; and increased mitochondrial activity. All these changes contribute to improve pain, quality of sleep, fatigue, anxiety, and other symptoms. The possibility of socialization, depending on the circumstances, and the positive influence on some psychological aspects should also be taken into account. Physical activity has represented the most frequently employed and studied non-drug intervention for FM. However, the most appropriate type has not been established, as well as the optimal frequency and intensity[48].

Psychological aspects should always be evaluated and occasional disorders should be identified, aiming at real support and specialized help as necessary. Sleep disturbances should also be approached and treated[54].

In a recent literature review, involving mainly systematic reviews and meta-analysis publications over last 12 years, a lack of uniformity on the type of rehabilitation and exercise that should be employed in this chronic pain syndrome was verified. The forms of aerobic activity studied (walking, marching, cycling, rowing, etc.) were varied, as well as other types of exercising (stretching, isometric and isokinetic exercises, among other exercises for muscular strengthening), and various forms of hydrotherapy (aquatic respiratory exercises, deep water running, hydrogymnastics, swimming, among others). A great diversity in rehabilitation methods, such as coping, biofeedback, family education, cognitive-behavioral therapy, and manipulation and relaxation techniques was also found. Overall, the studies concluded that the effects were beneficial both from exercises and from different types of rehabilitation, even if involving heterogeneous modalities[48].

Occupational aspects

Scientific literature offers no evidence that FM is occupational in origin. In the 1990's, some scientific papers related to occupational trauma and litigation involving FM were published[55-57].

However, literature data are not enough to establish causality. The connection with repetition microtrauma has been suggested by some authors; however, these studies were either conducted with small samples of patients or documented with isolated case reports[58,59].

FM does not usually lead to incapacity to work. In cases of significant pain or fatigue, taking a few sick days can be considered. Nevertheless, litigious repetitive requests of temporary leaves have been observed in judicial practice, resulting in a long and continued abscence of the patient. There is no systematic investigation of these lawsuits aiming to quantify how often this has occurred or how its economic dimension has impacted the social security system in Brazil. Data are empirical and observational. It cannot be denied that a protracted leave and the search for financial compensation in a chronic pain setting may be harmful, as investigations have demonstrated[60,61].

Of note, individuals with chronic pain are prone to persistence of painful symptomatology when they are involved in litigation[62]. In addition, there is increased malingering in a permissive system of judicial compensation[63,64].

It is debatable whether patients with fibromyalgia experience their symptoms worsened when their functions are performed under strict productivity criteria and pressured by time, such as in assembly lines. To date, the biomechanical limits of these patients have not been objectively defined, making it impossible to establish reduction, modification, or elimination criteria for any specific work setting. A worker with FM might keep performing his/her work, more slowly, with his/her productivity criteria or demands reconsidered.

Systematic reviews, such as that by Boocock et al., also establish that there is no current specific modification in work or labor intervention strategy that can be considered effective to solve the occupational issues involving these patients. The authors also mention the lack of research for several labor activities[65].

In FM, as in any other chronic pain syndrome, the sense of incapacity can be influenced by social and psychological factors. Work incapacity allegations may be vicious when psychological factors are predominant, or when pain or fatigue seems less severe than reported. The problem can become more pronounced when there is an interest in secondary gain. In settings where ensuring the absence of such interest is difficult to prove, the only solution is to keep a prolonged longitudinal follow-up, which improves doctor-patient relationship.

It is important to note that courts in the United States usually do not grant benefits to patients with FM[66].

These patients are prone to have their symptoms worsened when they present with associated psychological disorders. A study conducted in Brazil found that 30% of FM patients exhibited severe depression and 34%, moderate depression; this same study found that 70% of FM patients had traits of significant anxiety and 88% exhibited a high anxiety status[67].

Concerning depression, Brazilian labor laws have specific terms for this illness. However, it is imperative not to confuse depression with FM. A physician should not attempt to diagnose depression without having enough experience and without well-established diagnostic criteria.

If there is a significant level of depression, the possibility of a medical leave should be considered. However, the patient must not feel comfortable in this situation, due to the consequent creation of a vicious circle and no adherence to treatment.

Another noteworthy aspect is the possibility of malingering. In a controlled study involving FM patients, healthy controls and patients motivated to malinger, the American College of Rheumatology (ACR) criteria were found to be 80% accurate, with a good agreement and reproducibility level towards tender points and control points so as to distinguish malingerers. This study's results demonstrate that there is no malingering test and it is likely a number of malingerers and true FM patients could remain unidentified[68].

Final considerations

FM is a syndrome with a prominently clinical diagnosis, characterized by chronic musculoskeletal pain associated with various symptoms. It may be confused with several rheumatic and non-rheumatic diseases. An individualized and multidisciplinary approach, combining drug and nondrug treatment, is required.

There is no scientific evidence determining that FM is caused by work. However, reasonable labor adaptations should be sought, including reduced time for task execution, among others, although labor modifications for this disease are not yet defined.

If the patient with fibromyalgia presents significant levels of pain or fatigue and does not respond to appropriate treatment, a short medical leave could be considered, although repetitive temporary leaves obtained by litigious means have been empirically observed, but they have no scientific support for their real requirement and their consequent economic repercussions. There is negative evidence for patients regarding litigation and long leaves. Prolonged leaves are justified in the case of associated severe depression.

When approaching patients with fibromyalgia, it is important to explain this chronic pain syndrome and the barriers against clinical improvement.

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